EXHIBIT 5

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PATENTS
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July 14, 2004

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Re: Inventorship Review for U.S. Serial No. 09/930,915 for IMMUNOGENIC HBc CHIMER PARTICLES HAVING ENHANCED STABILITY; and U.S. Serial No. 09/931,325 for MALARIA IMMUNOGEN AND VACCINE

Dear Ed and Tom:

Pursuant to a request by Apovia, Inc. I have reviewed the subject applications, U.S. provisional application Serial No. 60/225,813, International Patent Application No. PCT/US01/25625, documents supplied by Dr. David R. Milich, and have spoken with Drs. Ashley J. Birkett, David R. Milich, as well as George B. Thornton, with a view toward determining whether Dr. Milich qualifies as a co-inventor with Dr. Birkett for the subject matter claimed in the above-identified applications.

OPINION

1. As presently advised, Dr. Milich does not qualify as co-inventor with Dr. Birkett for the invention claimed in U.S. Serial No. 09/930,915.

2. As presently advised, Dr. Milich does not quality as co-inventor with Dr. Birkett for the invention claimed in U.S. Serial No. 09/931,325.

REASONS FOR THE OPINION

Applicable Law

The threshold issue in determining inventorship is conception. One does not qualify as an inventor unless he/she participates in the conception of the claimed invention. Ethicon, Inc. v. United States Surgical Corp. 135 F.3d 1456, 1460, 45 U.S.P.Q.2d 1545, 1548 (Fed. Cir. 1998).

The conception of an invention consists of the complete performance of the mental part of the inventive act. All that remains to be accomplished in order to perfect the act or instrument belongs to the department of construction, not invention. It is, therefore, the formation in the mind of the inventor of a definite and permanent idea of the complete and operative invention as it is thereafter to be applied in practice that constitutes a conception within the meaning of the patent law. Mergenthaler v. Scudder, 11 App. D.C. 264, 276 (D.C. Cir. 1897). The test for conception is whether the inventor had an idea that was definite and permanent enough that one skilled in the art could understand the invention. Burroughs Wellcome Co. v. Barr Laboratories, Inc., 40 F.3d 1223, 1228, 32 U.S.P.Q.2d 1915, 1919 (Fed. Cir. 1994). An idea is definite and permanent when the inventor has a specific, settled idea, a particular solution to the problem at hand, not just a general goal or research plan he hopes to pursue. Id., citing Fiers v. Revel, 984 F.2d 1164, 1169 (Fed. Cir. 1993).

Joint inventors are those who collaborate to bring about the final invention, each contributing in some manner to its conception. Burroughs Wellcome, 40 F.3d at 1227, 32 U.S.P.Q.2d at 1919. One does not qualify as a joint inventor merely by assisting an actual inventor. Board of Education v. American Bioscience, 333 F.3d 1330, 1338, 67 U.S.P.Q.2d 1252, 1257 (Fed. Cir. 2003). "One who simply provides the inventor with well-known principles or explains the state of the art without ever having 'a firm and definite idea' of the claimed combination as a whole does not qualify as a joint inventor." Ethicon, 135 F.3d at 1460, 45 U.S.P.Q. at 1548 (quoting O'Reilly v. Morse, 56 U.S. (15 How.) 62, 111 (1853)). Teaching skills or general methods that somehow facilitate a later invention, without more, do not render one a co-inventor. Board of Education, 333 F.3d at 1342, 67 U.S.P.Q.2d at 1261. Also, general knowledge regarding the anticipated biological properties of groups of complex chemical compounds is insufficient to confer inventorship status with respect to specifically claimed compounds. Amgen, Inc. v. Chugai Pharmaceutical Co., 927 F.2d 1200, 1206, 18 U.S.P.Q.2d 1016, 1021 (Fed. Cir. 1991).

Conception of an invention must be independently corroborated. Price v. Symsek, 988 F.2d 1187, 1194, 26 U.S.P.Q.2d 1031, 1036 (Fed. Cir. 1993). Unauthenticated laboratory

notebook pages do not satisfy the corroboration rule. Dentsply Research & Development v. Cadco Dental Products, 14 U.S.P.Q.2d 1039, 1042 (C.D. Cal. 1989).

The Facts

The patent applications here under consideration relate to specific modified immunogenic hepatitis B core (HBc) proteins that have been engineered for the display of an immunogenic epitope (antigenic determinant) (U.S. Serial No. 09/931,325) as well as enhanced stability of self-assembled particles (U.S. Serial No. 09/930,915) that include these particular HBc proteins. The claims in these patent applications (Appendix A) are directed to immunogens based on the specifically modified HBc protein, polynucleic acids encoding same, host cells transformed with such nucleic acids, and to methods for inducing an immune response utilizing the aforementioned immunogens.

Unmodified HBc protein is a known immunogenic carrier that stimulates the T-cell response. See, for example, U.S. Patent No. 5,143,726 to Thornton, Moriarty, Milich, McLachlan. (Appendix B, Document 1). Thus, patentability of the claims in U.S. Serial No. 09/930,915 and U.S. Serial No. 09/931,325 necessarily must be based on the specific modifications that have been made to the HBc protein.

In December 1997, Dr. Ashley J. Birkett of ICC/Synthetic Genetics (predecessor in interest of Apovia Inc.) submitted a Grant Application for the development of a malaria vaccine which utilizes HBc protein as an immunogenic carrier for epitopes specific to malaria. (Appendix B, Document 2). The grant application discusses in detail the state of the art and the contemplated research plan. Dr. Milich is listed as a consultant.

The time frame for this project was stated as 7/1/98 through 12/31/98. (Appendix B, Document 2).

Dr. Milich was retained by ICC as a consultant on the HBc antigen as an epitope carrier. (Appendix B, Document 3). The use of HBc antigen as an epitope carrier was known in the art at that time (Appendix B, Documents 4 and 5).

The consultancy period for Dr. Milich was one year from January 1, 1998; this overlaps the time frame for the malaria vaccine project. (Appendix B, Document 3).

Paragraph 7 of Dr. Milich's Consulting Agreement obligates him to disclose to ICC, in writing, all inventions, patentable or not, conceived or first reduced to practice by Dr. Milich alone or in collaboration with others during the consultancy period, and for a one-year

time period thereafter. That is, from January 1, 1998 to January 1, 2000. No such written disclosures by Dr. Milich have been identified, however.

In a letter dated March 23, 2000 by Dr. Milich to Dr. Thornton (Appendix B, Document 6), Dr. Milich contends that "[t]he immunologic analysis allowed Ashley and I to constantly design, test and improve one construct after another, which ultimately led to the production of stable HBc Ag-hybrid particles and to the design of the final vaccine candidate (i.e., PF3.1)." This letter, however, does not provide any evidence of any specific contribution by Dr. Milich to the conception of the particular modified HBc proteins that are defined by the claims in the subject patent applications.

No documentation has been identified by Dr. Milich or anyone else to show or identify a specific contribution made by Dr. Milich to the conception of the claimed modified HBc proteins, polynucleic acids encoding same, or their uses. It appears that the proteins were made by Dr. Birkett and were tested in Dr. Milich's laboratory for stability, antigenicity, and immunogenicity. Copies of the test data and other documents made available, however, are undated and unsigned. There also is no indication as to who performed the assays.

No corroborating evidence has been produced showing any contribution by Dr. Milich to the conception of the claimed modified HBc proteins, polynucleic acids encoding same, or their uses.

International Patent Application No. PCT/US01/25625 is based on U.S. provisional application Serial No. 60/225,813 and U.S. utility application Serial No. 09/931,325, and claims priority of both. United States is not a designated State in Application No. PCT/US01/25625. According to PCT Rule 4.1(a)(v), indication concerning inventorship is mandatory only where at least one State requires the inventor's name to be furnished at the time of filing a national application. At the time of the International Filing Date, 16 August 2001, United States was the only State with such a requirement. Moreover, the time period for national filings based on Application No. PCT/US01/25625 has expired. Thus, the inventorship issue vis-a-vis Application No. PCT/US01/25625 is deemed moot.

CONCLUSION

While Dr. Milich as a consultant may have contributed his already accumulated knowledge to Dr. Birkett's project, no evidence has been provided to establish that Dr. Milich had made an inventive contribution to the claimed invention. Absent any documentation or testimony that would establish, at least by a preponderance of evidence, Dr. Milich's purported contribution to the conception of the invention as defined by the claims in the subject patent

applications, and an independent corroboration thereof, his status as a co-inventor cannot be justified.

Very truly yours,

OLSON & HIERL, LTD.

By
Talivaldis Cepuritis

TC:psz
Enclosures: Appendices A & B

cc: Maha A. Hamdan, J.D., Ph.D. (w/enc.)

APPENDICES

Inventorship Review for U.S. Serial No. 09/930,915
for IMMUNOGENIC HBc CHIMER PARTICLES
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